Efficacy of a combined oral contraceptive containing 0.030 mg ethinylestradiol/2 mg dienogest for the treatment of papulopustular acne in comparison with placebo and 0.35 mg ethinylestradiol/2 mg cyproterone acetate, Palombo-Kinne E, Schellhmidt I, Graeser T. Contraception 2009; 79: 282–289

A recent Cochrane Review found that combined oral contraceptives (COCs) reduced acne lesion counts, severity grades and self-assessed acne compared to placebo. However, differences in the comparability of the COCs with varying progestin types and dosages were less clear.

Ethinylestradiol (EE) and cyproterone acetate (CPA) are used as a hormonal treatment for acne, due to its anti-androgenic action. The British National Formulary (BNF) states that it can be a useful treatment option for women who also require oral contraception.

The authors of this study report on a drug company-funded, randomised, double-blind, three-arm study that recruited healthy women aged 16–45 years with mild to moderate facial acne from 65 centres in eastern Europe and the Russian Federation. Their aim was to determine whether a COC-containing dienogest (DNG) would be effective and non-inferior to EE/CPA in the treatment of mild to moderate acne.

Participants were allocated to six cycles of treatment: EE (2 mg / 0.035 mg) (n = 514) or placebo (n = 267). Primary outcome measures were the percentage change of inflammatory and total lesion counts, and the percentage of patients with improvements according to the Investigator Global Assessment.

The authors state that all primary analyses provided evidence that EE/DNG was superior to placebo and non-inferior to EE/CPA (p<0.05). For total lesion count the percentage change (±SD) from baseline to cycle six was: 54.7 ± 26.3% (n = 515) for EE/DNG, –33.6 ± 33.6% (n = 268) for EE/CPA and –39.4 ± 33.6% (n = 259) for placebo.

Points to note include the fact that this study was concerned with treatment of mild to moderate acne, whereas the BNF states that EE/CPA is licensed for women with severe acne not responding to oral antibacterial treatment. In addition, patients who were not to treat analysis was not used. Although a statistically significant (p<0.05) difference was found between the means of all three primary outcome measures of the high-dose EE/DNG, the percentage of patients of EE/DNG, given the large placebo effect it is unclear whether this equates with a clinically significant difference.

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Reference


Presently the treatment regimen for termination of early pregnancy (less than 63 days gestation) in the UK comprises 200 mg mifepristone orally followed by 800 µg misoprostol vaginally 36–48 hours later. Although unlicensed, these are the guidelines from the Royal College of Obstetricians and Gynaecologists (2004) for regimens for inducing medical abortion. The mifepristone works to soften and dilate the uterine cervix and sensitize the myometrium prior to the administration of the prostaglandin analogue, misoprostol. Pharmacokinetic studies suggest that oral administration of 100 mg or higher single doses of mifepristone result in similarly efficacious serum concentrations. Data available regarding the optimal interval and number of administrations suggest that the efficacy is highest when the interval is 48 hours. No research studies have previously investigated the time interval between doses, or the comparison of the 100 mg with 200 mg mifepristone, to 2 mg misoprostol given after 24 or 48 hours to which 2126 women were randomised, across 13 obstetric and gynaecology departments in nine countries.

Through a thorough selection protocol almost equal numbers (with significant similarities in baseline characteristics and previous termination numbers) were recruited to each arm across all sites; randomisation was achieved by utilisation of an international sequence produced by the World Health Organization in Geneva. The double-blind nature was designed and powered with a low attrition rate (55 from 2181 women). Even those patients who lost follow-up are counted as failures of method when in fact they may have had complete abortions. Internal validity was achieved by randomisation and a required confidence interval of 95% for the difference in complete abortion rates – the margin of equivalence of 5% having been chosen using the researchers’ clinical judgement. External validity was demonstrated as women were enrolled from several different populations and included clinicians with different levels of experience of medical abortions.

The primary outcome measure was efficacy of the treatment in inducing complete abortion in all arms. The study found that both doses and both administration intervals are equivalent when terminated by 50 days post conception. With results were inconclusive when the gestational age is 50 days or more. The findings show similar efficacy for complete abortion with both mifepristone doses and both treatment intervals. Despite the maximal sensitivity of mifepristone on days 6–7 before the prostaglandin analogue use, this study found the 24-hour interval to have lower failure rates than the 48-hour interval group. Also both mifepristone doses produced equivalent rates of failure to achieve complete abortion within each interval of misoprostol administration. Reports of side effects were lower in the 24-hour interval group, suggesting this regimen could be better tolerated and provide a more pleasant patient experience. Overall conclusions are that the dose of mifepristone could be lowered to 100 mg and the administration interval between that and 800 µg misoprostol could be shortened to 24 hours without detrimental effect when terminating early pregnancy. This could have many repercussions in termination service including reducing cost implications of higher doses and the provision of well-tolerated regimens.

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Diola if aggravation, exacerbation or new risks appear. No epidemiological studies on the effects of estradiol/estradiol valerate containing COCs exist. All of the following warnings and precautions are derived from the limited data of ethinylestradiol-containing COCs. Whether these warnings apply to Diola is unknown. Some studies suggest an association between COCs and venous and arterial thromboembolism. Risk for venous thrombosis associated with COCs increases with: age, family history of VTE, immobility, surgery, major trauma, obesity. There is an increased risk of VTE for any reasons associated with a higher degree of risk in the first year of COC use but still much lower than that associated with pregnancy. VTE can be fatal. The risk of VTE for Diola use is currently unknown. Risk for thrombosis or a cerebrovascular accident increases with: age, smoking, family history of arterial thrombembolism, obesity, polycystic ovarian disease, migraines, valvular heart disease, atrial fibrillation. Advise users to contact a doctor at first sign of possible thrombosis (e.g. chest or limb pain, breathing difficulties, etc.). If thrombosis suspected or confirmed, stop COC use; consider increased risk during the puerperium. Diabetes, systemic lupus, erythematosus (SLE), Sjogren’s syndrome (SS), Human Immunodeficiency Virus (HIV), chronic inflammatory bowel disease and sickle cell disease are associated with increased risk of vascular events. Most medical management options require strict medical supervision. Interactions: Interaction with specific drugs will necessitate additional non-hormonal contraceptive measures. Diola use with other medicines. Undesirable effects: Common - Headache (including tension headache), abdominal pain (including abdominal distension), acne, weight increase. Serious side effects include: Acute intracerebral bleeding (metrorrhagia), breast discomfort, weight increase. Serious side effects include: Acute intracerebral bleeding (metrorrhagia), breast discomfort, weight increase. Serious side effects include: Acute intracerebral bleeding (metrorrhagia), breast discomfort, weight increase. Serious side effects include: Acute intracerebral bleeding (metrorrhagia), breast discomfort, weight increase. Serious side effects include: Acute intracerebral bleeding (metrorrhagia), breast discomfort, weight increase. Serious side effects include: Acute intracerebral bleeding (metrorrhagia), breast discomfort, weight increase. Serious side effects include: Acute intracerebral bleeding (metrorrhagia), breast discomfort, weight increase. Serious side effects include: Acute intracerebral bleeding (metrorrhagia), breast discomfort, weight increase. Serious side effects include: Acute intracerebral bleeding (metrorrhagia), breast discomfort, weight increase. Serious side effects include: Acute intracerebral bleeding (metrorrhagia), breast discomfort, weight increase. Serious side effects include: Acute intracerebral bleeding (metrorrhagia), breast discomfort, weight increase. Serious side effects include: Acute intracerebral bleeding (metrorrhagia), breast discomfort, weight increase. Serious side effects include: Acute intracerebral bleeding (metrorrhagia), breast discomfort, weight increase. Serious side effects include: Acute intracerebral bleeding (metrorrhagia), breast discomfort, weight increase. Serious side effects include: Acute intracerebral bleeding (metrorrhagia), breast discomfort, weight increase. Serious side effects include: Acute intracerebral bleeding (metrorrhagia), breast discomfort, weight increase. Serious side effects include: Acute intracerebral bleeding (metrorrhagia), breast discomfort, weight increase. Serious side effects include: Acute intracerebral bleeding (metrorrhagia), breast discomfort, weight increase. Serious side effects include: Acute intracerebral bleeding (metrorrhagia), breast discomfort, weight increase. Serious side effects include: Acute intracerebral bleeding (metrorrhagia), breast discomfort, weight increase. Serious side effects include: Acute intracerebral bleeding (metrorrhagia), breast discomfort, weight increase. Serious side effects include: Acute intracerebral bleeding (metrorrhagia), breast discomfort, weight increase. Serious side effects include: Acute intracerebral bleeding (metrorrhagia), breast discomfort, weight increase. Serious side effects include: Acute intracerebral bleeding (metrorrhagia), breast discomfort, weight increase. Serious side effects include: Acute intracerebral bleeding (metrorrhagia), breast discomfort, weight increase.